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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,377	06/28/2005	Yoshiaki Nabuchi	NABUCHI1	3839

1444 7590 02/02/2010

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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
02/02/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,377	NABUCHI ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,6,9-12 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,6,9-12 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

First Office Action on the Merits of a RCE

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 14, 2009 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Application

3. Claims 2, 3, 6, 9-12 and 15-18 are pending in the present application. The instant claims stand rejected as indicated below.

Claim Rejections - 35 USC § 112

4. The rejection of claims 13 and 14 under 35 USC 112, 1st paragraph, scope of enablement is made moot by the cancellation of the instant claims.

Claim Objections

5. The objection to claims 7, 8, 13 and 14 under 37 CFR 1.75(c), as being of improper dependent form is made moot by the cancellation of the instant claims.

Double Patenting

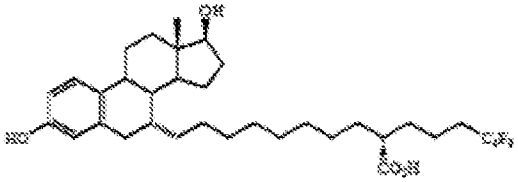
6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

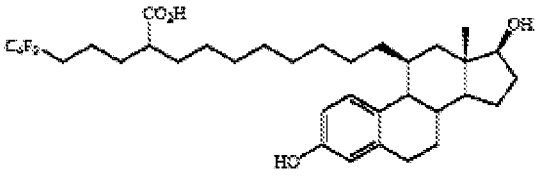
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 2, 3, 6, 9-12 and 15-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,737,417. Although the conflicting claims are not identical, they are not patentably distinct from each other because each is directed to estrogens having

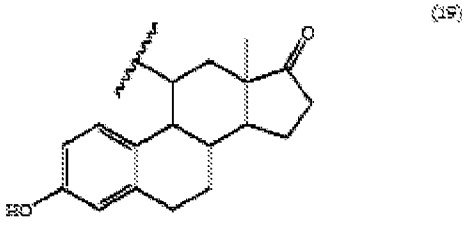
attached to either the 7- or 11-position of the steroid moiety. The claims of the cited patent differ from the instant claim in the recitation of (a) the scope of the recited compounds and (b) the method of treating osteoporosis. However, (a) the scope of the instantly claimed compounds is rendered obvious by the exemplification of compounds such as:

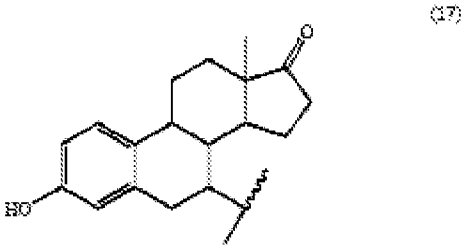


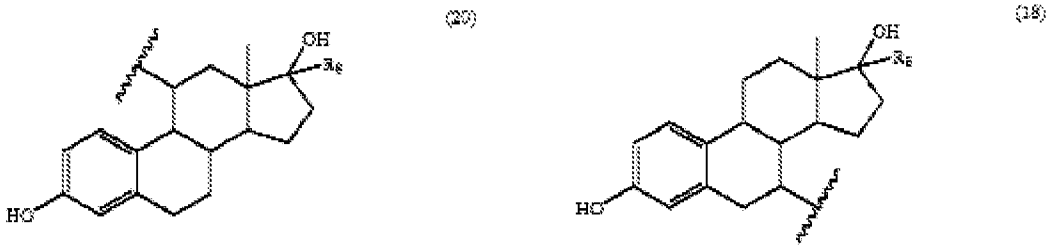
and



(see for example, Table 1 of the cited patent) and the disclosure of steroidal moiety such as:







(see for example, claim 1 of the cited patent) and (b) the method of treating osteoporosis is rendered obvious by the teachings of the prior art as to the use of anti-estrogenic compounds in the treatment of breast cancer (see claims 24-27 of the cited patent) and osteoporosis (see Young, US 4,894,373, Abstract; col. 1, lines 14-16).

Claim Rejections - 35 USC § 103

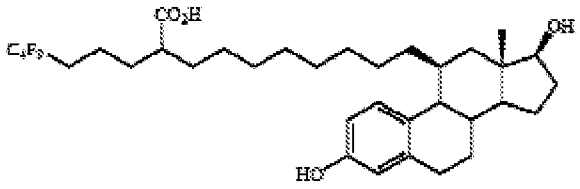
8. The rejection of claims 7, 8, 13 and 14 under 35 USC 103(a) over Jo et al. (WO 0142186, see English translation US 6,737,417) is made moot by the cancellation of the instant claims.

9. The rejection of claims 2, 3, 6 and 9-12 under 35 USC 103(a) over Jo et al. (WO 0142186, see English translation US 6,737,417) is maintained and claims 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jo et al. (WO 0142186, see English translation US 6,737,417).

Applicant argues the claimed compound, as represented by Compound 12b, have a higher and more potent pharmacological efficacy in oral administration as compared to the prior art compound and, thus, are not obvious in light of the disclosure

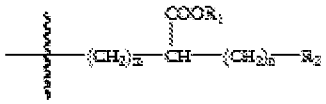
of the cited reference. Applicant's argument was considered but not persuasive for the following reasons.

First, the data does not commensurate in scope with the claimed invention. The comparison was made between the claimed 17-oxo and the exemplified prior art 17-hydroxy compounds. However, the claimed invention is inclusive of the corresponding 17-hydroxy,17-ethynyl-derivative as well as compounds having said 2-(4,4,5,5,6,6,7,7,7-nonafluorheptyl)decanoic acid attached to the 11-position as shown in prior art compound below:



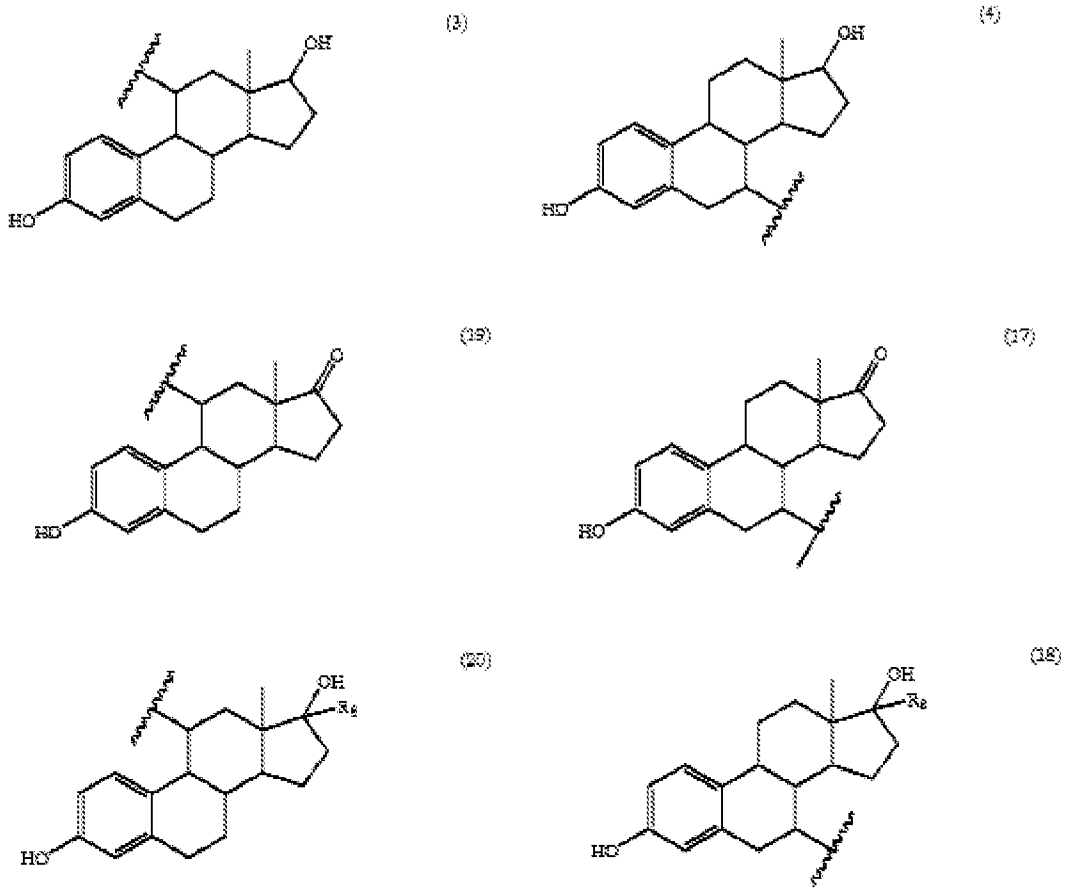
(see Table 1, compounds 20, 22,. 23, 25 and 39).

Second, Jo teaches anti-estrogenic compounds having a side chain of formula (I)



in which
R_1 represents a hydrogen atom, etc.,
R_2 represents a C_1–C_7 halogenoalkyl group, etc.,
m represents an integer of 2 to 14, and
n represents an integer of 2 to 7,

allowed said compounds to show a significantly increased in activity by oral route (see col. 3, lines 8-13). Said compounds are inclusive of the prior art compounds wherein A is:

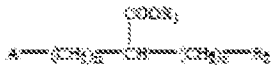


(see claim 1 of the cited reference).

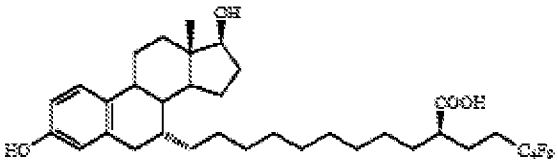
Thirdly, the skilled artisan in the art would know that there is a difference in the bioavailability of estradiol, estrone and ethynyl estradiol after oral administration. For example, the art teaches the bioavailability of ethynyl estradiol is improved over estradiol after oral administration (see for example, US 4,757,062, col. 3, lines 28-35). Based on what the skilled artisan in the art knew at the time of present invention, he would have the reasonable expectation that (a) estradiol, estrone and ethynyl estradiol having the side chain of the cited reference would have increased oral bioavailability

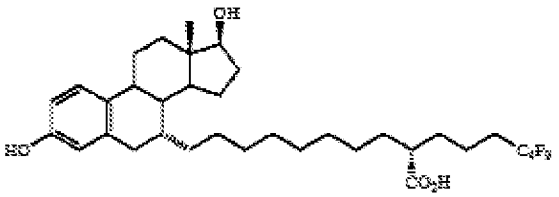
over the estradiol, estrone and ethynyl estradiol and (b) that there would be differences in the bioavailability of said compounds after oral administration.

Lastly, applicant's argument as to the definition of "A" and the variation of substituents thereon in general formula 2:

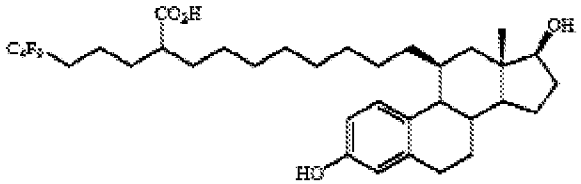


of Jo is noted. However, the issue is not the scope of the prior art compound but the guidance provided by the reference to skilled artisan in the art at the time of the present invention to enable said artisan to obtain the claimed compound(s). As stated in the previous Office Action, the reference exemplifies compounds such as





and

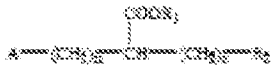


(see cols. Table 1, Examples 15, 16, 18-20, 22, 23, 25, 36-39) and teaches "A" is inclusive of the corresponding 17-oxo as well as the 17-akylnyl, 17-hydroxyl derivatives and, thus, there is direction in the cited prior art to make the claimed compound(s).

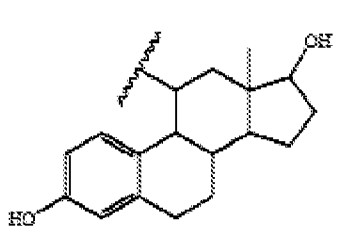
For these reasons and those given in the previous Office Action, the rejection of claims 2, 3, 6 and 9-12 under 35 USC 103(a) over Jo et al. (WO 0142186, see English translation US 6,737,417) is maintained and claims 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jo et al. (WO 0142186, see English translation US 6,737,417).

10. Claims 2, 3, 6, 9-12 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jo et al. (WO 0142186, see English translation US 6,737,417) in view of Matsuda et al. (US 4,888,323), Young (US 4,894,373) and Aungst et al. (US 4,757,062).

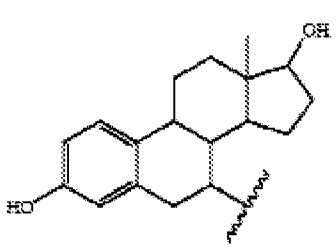
Jo et al. teaches compounds with hydroxycarbonyl-halogenoalkyl derivatives side chain of the formula:



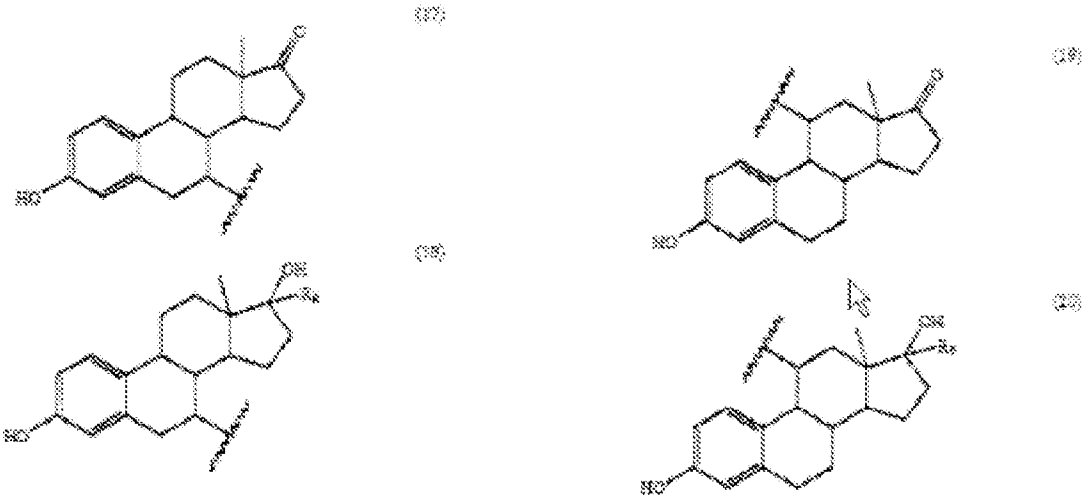
having increased activity after oral administration (see the entire article, especially Abstract; col. 4, line 22 - col. 8, line 55). The reference teaches A groups such as



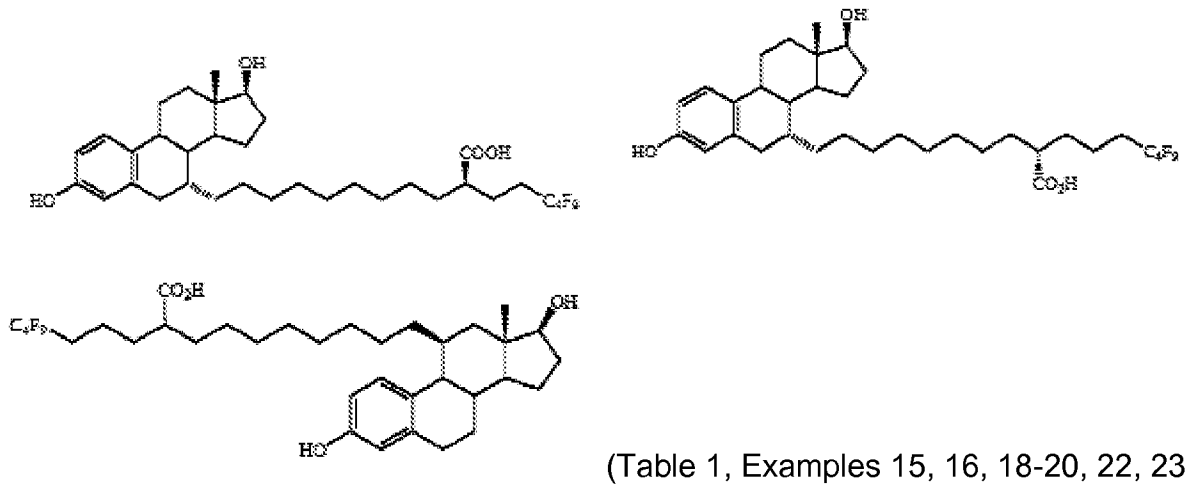
(3)



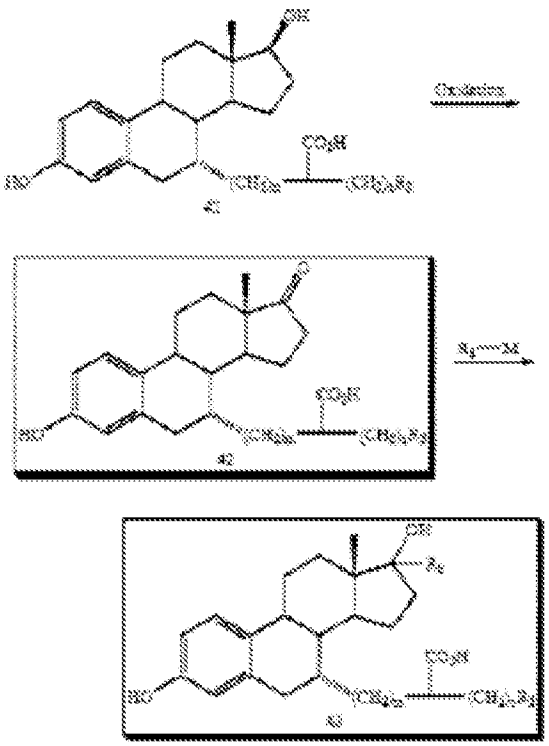
(4)



wherein R_8 represents saturated or unsaturated alkyl groups such as C_1-C_5 alkyl, C_2-C_5 alkenyl or C_2-C_5 alkynyl (see col. 8, lines 35-38). The reference exemplifies compounds such as



(Table 1, Examples 15, 16, 18-20, 22, 23, 25, 36-39). Jo also teaches processes such as (a) oxidation of the 17-hydroxyl group by Jones oxidation, PCC oxidation, etc. to produce the corresponding 17-oxo derivative and (b) the alkylation of the 17-oxo derivative with R_8-M wherein R_8 is as defined above and M is a metal with the production of the 17-hydroxy-17-alkyl-derivative (see below):



(see col. 26, Scheme 9; Process 9, col. 44, lines 9-23).

The instant claims differ from the reference by reciting compounds not exemplified by Jo et al., i.e., 17-oxo or 17-hydroxyl-17-ethynyl derivatives. However, the reference teaches said 17-substituents (see A groups above) and, therefore, the claimed compounds would have been obvious to the ordinary artisan in the art at the time of the present invention. The motivation would have been on the desire to increase activity of the compounds after oral administration as taught by Jo et al. Additionally, the art teaches differences in the bioavailability of estrogens such as estradiol, estrone and ethynyl estradiol. For example, **Aungst** et al. teaches ethynyl estradiol has improved bioavailability over estradiol after oral administration (see col. 3, lines 28-35). Based on said, the skilled artisan would have the reasonable expectation that there

would be differences in the bioavailability of the different estrogens encompassed by the genus of Jo. Based on the teachings of Aungst as stated above, the skilled artisan in the art at the time of the present invention would have the reasonable expectation that the bioavailability of the ethynyl estradiol derivative of Jo would be higher than the corresponding estradiol derivative after oral administration.

Claim 10 further differs from the reference by reciting the oxidation reaction is performed by Oppenauer oxidation. However, Oppenauer, like Jones oxidation, PCC oxidation and Swern oxidation, is a conventional oxidation method known in the chemical art (see for example, **Matsuda**, US 4,888,323: col. 3 lines 31-36) and, thus, the skilled artisan would have the reasonable expectation that Oppenauer oxidation would also be useful in the oxidation process as taught by Jo.

Claims 15 and 17 further differ from the reference by reciting the treatment of osteoporosis. However, the use of anti-estrogenic compounds in the treatment of osteoporosis is well known in the art (see for example, **Young**, US 4,894,373, Abstract; col. 1, lines 14-16).

Telephone Inquiry

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. 2Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1628